

Persistent Hiccups After Diaphragmatic Plication Despite Previous Phrenic Nerve Sacrifice

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Case Report

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Abstract

Background

Persistent hiccups are an uncommon but potentially disabling complication after thoracic surgery. Their pathophysiology remains incompletely understood and involves a complex reflex arc including phrenic, vagal, and sympathetic afferent pathways. We report an unusual case of persistent hiccups occurring immediately after diaphragmatic plication of a previously denervated hemidiaphragm in a patient with myasthenia gravis.

Case presentation

A 53-year-old man with acetylcholine receptor antibody-positive myasthenia gravis underwent extended robotic thymectomy for recurrent thymoma, including intentional sacrifice of the left phrenic nerve. One year later, he developed progressive exertional dyspnea related to left diaphragmatic paralysis, with marked positional impairment on pulmonary function testing. Because of significant functional limitation, robotic left diaphragmatic plication was performed. Persistent hiccups developed immediately after surgery and were severe enough to interfere with sleep and oral intake. No metabolic, gastric, or medication-related trigger was identified. Despite previous phrenic nerve sacrifice, a postoperative reflex-mediated mechanism involving residual or alternative afferent pathways was suspected. Baclofen was considered undesirable because of the patient's myasthenia gravis and impaired respiratory mechanics. Low-dose gabapentin was therefore initiated, resulting in progressive improvement and complete resolution of hiccups within 96 hours at a dose of 200 mg daily, without respiratory deterioration or myasthenic exacerbation. No recurrence was observed at 6-week follow-up.

Conclusion

Persistent hiccups may occur after diaphragmatic plication despite previous ipsilateral phrenic nerve sacrifice, suggesting that diaphragmatic motor denervation does not abolish all sensory pathways capable of activating the hiccup reflex. Gabapentin may represent a useful therapeutic option in selected patients with myasthenia gravis when baclofen is considered undesirable, although careful clinical monitoring remains warranted.

Background

Hiccups are a common reflex phenomenon that is usually transient and self-limiting. However, persistent or intractable hiccups may become clinically significant, causing sleep disturbance, impaired oral intake, exhaustion, aspiration risk, and respiratory compromise [1, 2]. Their pathophysiology remains incompletely understood and is generally attributed to activation of a complex reflex arc involving peripheral afferent pathways, central integration within the brainstem and upper cervical spinal cord, and efferent activation of the diaphragm [1, 3].

The afferent limb of this reflex is thought to involve the phrenic, vagal, and sympathetic pathways [1, 3]. Accordingly, a wide range of thoracic and upper abdominal stimuli may precipitate hiccups. In the postoperative setting, diaphragmatic or pleural irritation, mediastinal manipulation, gastric distension, metabolic abnormalities, and vagal stimulation have all been implicated [1, 2]. Persistent postoperative hiccups remain uncommon, however, and their underlying mechanism is often difficult to establish.

Treatment is largely empirical. Baclofen, gabapentin, chlorpromazine, and metoclopramide are among the pharmacological agents most frequently reported, although the available evidence supporting their use remains limited [1, 4]. The choice of treatment may be particularly challenging in patients with underlying neuromuscular disease or impaired respiratory function.

The phrenic nerve plays a central role in both diaphragmatic motor innervation and the hiccup reflex. Whether previous phrenic nerve sacrifice prevents hiccups arising after subsequent diaphragmatic manipulation has not been established. We report a case of persistent hiccups occurring immediately after robotic plication of a chronically paralyzed hemidiaphragm following intentional phrenic nerve sacrifice during extended thymectomy in a patient with myasthenia gravis.

Case presentation

A 53-year-old man with acetylcholine receptor antibody-positive myasthenia gravis, clinically stable while receiving azathioprine and corticosteroids, was referred to our tertiary thoracic oncology center for suspected recurrent thymoma (Fig. 1). He had previously undergone right thoracoscopic thymectomy at another institution in 2011, although the original histopathological report was unavailable.

Reoperative surgery was performed using an extended robotic thymectomy with an “outside-the-cage” approach, as previously described for radical mediastinal surgery requiring en bloc resection of adjacent structures while minimizing intercostal trauma [5]. Resection included all mediastinal fat, a pericardial patch, wedge resection of the left upper lobe, intentional sacrifice of the left phrenic nerve, and separate right apical parietal pleural resection. A small right pleural lesion was also incidentally identified and resected. Histopathological examination demonstrated a 5.5-cm mixed B2/B3 thymoma encasing the left phrenic nerve without direct neural invasion. Resection margins were otherwise free. The pleural lesion confirmed metastatic thymoma, corresponding to modified Masaoka-Koga stage IVa disease.

Postoperative recovery was uncomplicated. Following multidisciplinary tumor board discussion, the patient subsequently underwent thoracoscopic hyperthermic intrathoracic chemotherapy for pleural metastatic disease, followed by adjuvant mediastinal radiotherapy. During oncological follow-up, no recurrence was identified. Myasthenic symptoms progressively improved after thymectomy, allowing corticosteroid tapering and eventual discontinuation.

One year later, the patient reported progressive exertional dyspnea related to left diaphragmatic paralysis. Pulmonary function testing demonstrated marked positional impairment, with total lung

capacity decreasing from 4.54 L in the seated position to 2.10 L while supine, and vital capacity decreasing from 4.17 L to 1.90 L.

Because symptoms significantly impaired quality of life, robotic left transthoracic diaphragmatic plication was performed. After extensive pneumolysis, the diaphragm was plicated using interrupted non-absorbable sutures reinforced with Teflon pledgets. Pre- and postoperative chest radiographs are shown in Fig. 2.

The immediate postoperative course was otherwise uncomplicated. However, persistent hiccups developed on postoperative day 0. Episodes were frequent and exhausting and interfered with both sleep and oral intake. No metabolic, gastric, or medication-related trigger was identified.

Given the close temporal relationship with diaphragmatic plication, a postoperative reflex-mediated mechanism involving residual or alternative afferent pathways was suspected. Baclofen was considered but avoided because of the patient's history of myasthenia gravis and impaired respiratory mechanics. Low-dose gabapentin was initiated instead. Symptoms progressively improved and completely resolved within 96 hours at a dose of 200 mg daily. No respiratory deterioration or myasthenic exacerbation occurred. At 6-week follow-up, hiccups had not recurred.

Discussion and Conclusions

This case is unusual because persistent hiccups occurred immediately after plication of a hemidiaphragm that had previously been denervated by intentional phrenic nerve sacrifice. Phrenic nerve section should theoretically abolish ipsilateral diaphragmatic motor innervation and substantially reduce phrenic afferent signaling. However, our observation suggests that previous phrenic nerve sacrifice does not preclude postoperative hiccup generation and that diaphragmatic motor denervation does not necessarily eliminate all sensory inputs capable of activating the hiccup reflex.

Several mechanisms may account for this apparent paradox. First, phrenic nerve sacrifice may not completely abolish afferent signaling. Proximal stump activity, residual neural fibers, or recruitment of collateral afferent pathways could theoretically contribute to postoperative reflex activation. Second, diaphragmatic and pleural sensation is not exclusively mediated by the phrenic nerve. Peripheral diaphragmatic regions, pleura, mediastinum, and pericardium may also provide sensory input through intercostal, vagal, or sympathetic pathways [1, 3]. In the present case, extensive pneumolysis, diaphragmatic retensioning, pledgeted sutures, and local postoperative inflammation may therefore have activated alternative afferent pathways despite prior phrenic nerve sacrifice.

Another possible explanation is that chronic diaphragmatic paralysis followed by abrupt mechanical retensioning during plication induced postoperative reflex hypersensitivity. The immediate onset of hiccups after surgery and their subsequent response to gabapentin are compatible with, although do not prove, a neuropathic or reflex-mediated mechanism. These hypotheses remain speculative, and a single

case cannot determine the relative contribution of residual phrenic afferents, alternative sensory pathways, or central sensitization.

Management of persistent hiccups remains largely empirical [1, 4]. Baclofen is one of the most frequently used pharmacological treatments and may act through gamma-aminobutyric acid B receptor agonism [6]. However, its sedative and muscle-relaxant effects may be undesirable in patients with myasthenia gravis or impaired respiratory reserve. Particular caution is warranted when prescribing drugs that may interfere with neuromuscular transmission in patients with myasthenia gravis [7]. In the present patient, baclofen was therefore avoided because of the underlying neuromuscular disease and impaired respiratory mechanics.

Gabapentin has been reported as an effective treatment for persistent or intractable hiccups, probably through modulation of abnormal neuronal excitability [4, 8]. However, exacerbation of myasthenia gravis associated with gabapentin has also been reported [9]. In the present patient, low-dose gabapentin achieved complete symptom resolution without respiratory deterioration or worsening of myasthenic symptoms. This case therefore suggests that gabapentin may represent a useful therapeutic option in carefully selected patients with myasthenia gravis when baclofen is considered undesirable, provided that neuromuscular and respiratory status are closely monitored.

This observation may also be relevant to thoracic oncology practice. Intentional phrenic nerve sacrifice may occasionally be required during radical resection of locally advanced thymic malignancies, and diaphragmatic plication may subsequently be considered in patients who develop symptomatic diaphragmatic paralysis. Surgeons should be aware that persistent hiccups may still occur after plication despite previous phrenic nerve sacrifice. More broadly, this case suggests that interruption of phrenic motor innervation does not necessarily abolish the afferent pathways capable of triggering the hiccup reflex.

Declarations

Ethics approval and consent to participate:

Not applicable.

Consent for publication:

Written informed consent for publication was obtained from the patient.

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Nothing to declare.

Author Contribution

SR and AS contributed to the collection of clinical data, the conception of the manuscript, and manuscript writing. All authors read and approved the final manuscript.

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Availability of data and materials:

The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

Competing interests: The authors declare that they have no competing interests.

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Figures

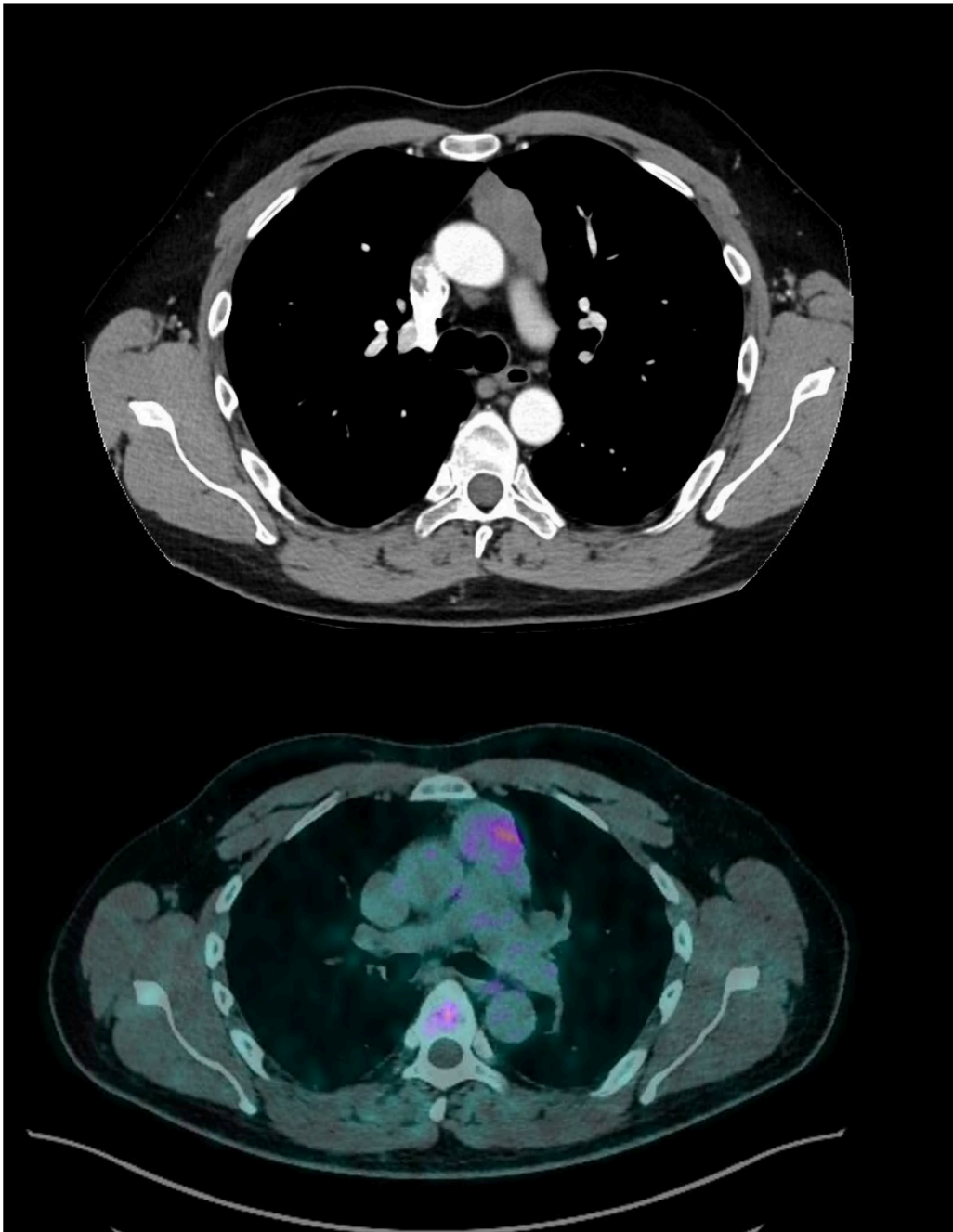


Figure 1

Preoperative CT and PET scan.

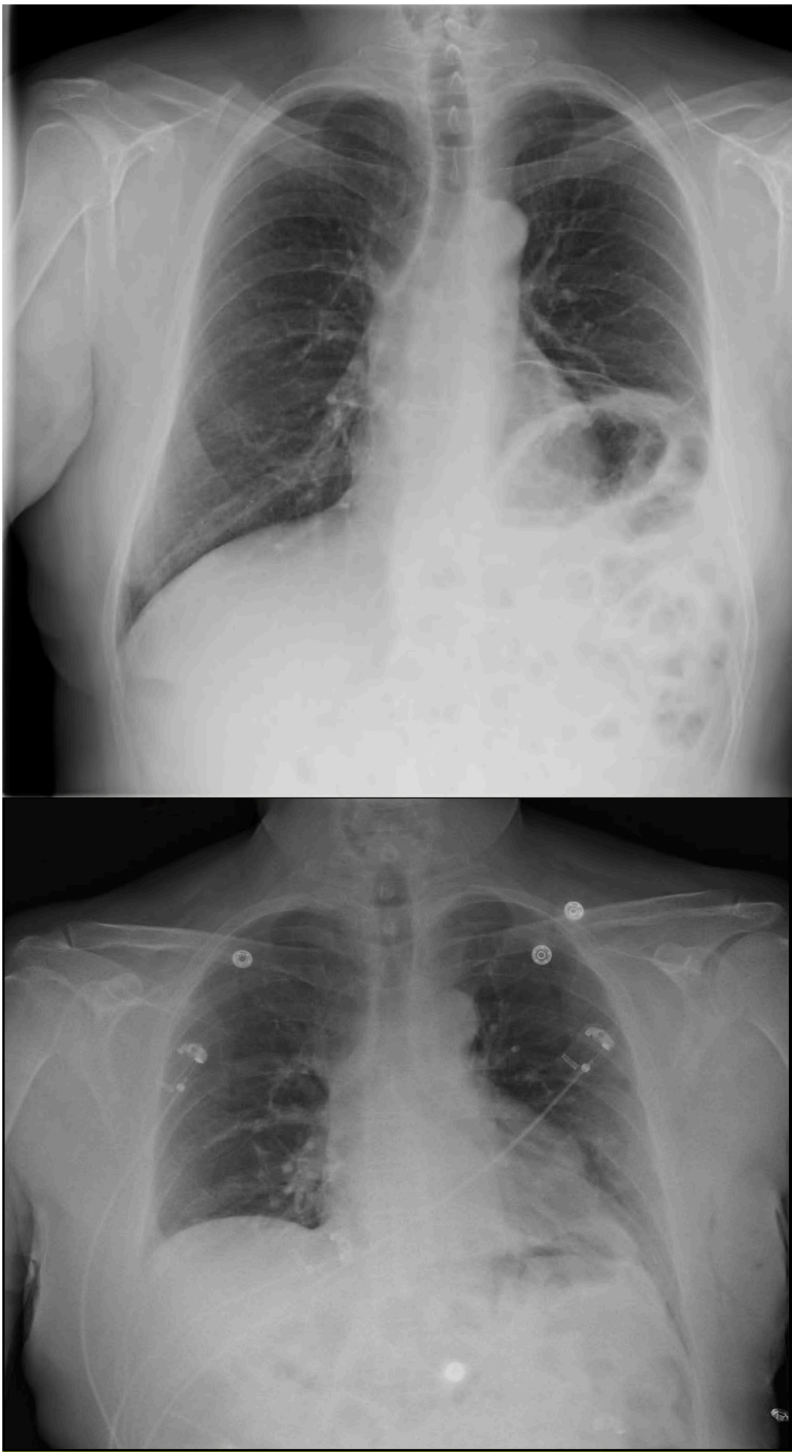


Figure 2

Pre- and postoperative Chest X-Rays